BACTERIOLOGICAL AND CLINICAL INVESTIGATIONS INTO THE NEW ANTISEPTIC DERMATOL.

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Last August, while looking over the Berliner klin. Wochenschrift, I saw the statement by Heinz in regard to an antiseptic powder which was to take the place of iodoform. And as the report showed that the material, a subgallate of bismuth which he called dermatol, had been produced after a long course of experimentation, during which many compounds had been tried, but rejected as unsuitable, I determined to try the dermatol during my Dispensary service, and see how my results would coincide with the claims made for it by Heinz. Accordingly I had the apothecary at the Dispensary secure a quantity. I began its use about the middle of September, 1891, and continued until the end of my service, January 1, 1892.

During all this time I used the gallate of bismuth in practically all the cases that presented themselves, where iodoform, aristol, or a simple, inert powder would have been indicated. During this time there were over 1300 new patients treated in the surgical department, so that I had abundant opportunity to observe where the new powder was useful, and where it was useless.

I purposely avoided reading any of the articles which appeared at various times upon the subject, so that I might be able to form an unbiased opinion as to its working. I found that my clinical observations were in almost complete harmony with the work already reported, while my laboratory experiments showed some points of difference.

The sub-gallate of bismuth was first produced in the Pharmatological Institute of the University of Breslau, and the preliminary report was made by Heinz and Liebrecht.

They had set themselves the task of producing a non-poisonous, bacteriacidal powder, which should aid wound healing after the manner of iodoform and aristol. To accomplish this, they tried, first of all, the other iodine compounds, and though many were found which were valuable in destroying germ life, yet the great ease with which they were broken up and yielded their iodine made them too dangerous to the patients. Iodoform alone appeared to have any stability. In none of their animal experiments were they able to find free iodine in the urine. The change probably only takes place if certain decomposing, aromatic bodies are present, which cause iodine to be set free.

After iodine, the phenol bases were tried throughout a long list, but these, too, had to be rejected, because of their irritating properties. Finally gallic was selected as the reducing agent, as it was non-poisonous, and present in 1-10 per cent. solution it was found to check entirely bacterial decomposition. Bismuth, after many experiments, was found to be the best element with which to combine the gallic acid.

That this compound was non-poisonous was proved by a large number of feeding experiments supplemented by subcutaneous and intra-peritoneal introduction of the material into animals, before it was used in the clinic.

The result of this patient, painstaking work was that the profession was given a saffron-yellow powder—

Insoluble in water, alcohol or ether,
Odorless,
Non-hygroscopic,
Astringent,
Non-poisonous,
Non-irritating,
Stable, being unaffected by steam or dry heat, in the process of sterilization, and having the power to check bacterial growth to a certain extent, though this was not claimed for it by its sponsors.

The opinions of various men who have used the subgallate of bismuth in their clinics is briefly as follows:

Dr. Sackur, surgical assistant at Breslau, considers it a ready, odorless, harmless material for advancing healing in all fresh, *aseptic*, and well-granulating wounds. On account of its drying properties and being absolutely non-irritating and non-poisonous, a sufficient quantity can be used to secure almost complete dryness of all wounds, and thus make the probability of healing without suppuration much greater.

2d. All phlegmonous conditions and freshly opened abscesses should, after being treated by free incision, be cleansed and dressed with moist antiseptic dressing before dermatol can be used. But when the wound is once cleansed, the healing is materially hastened by the dermatol dressing.

3d. It is of no value in torpid, slow granulating wounds and ulcers.

4th. No specific working against tubercular disease has been observed, as in the case of iodoform.

v. Rogner of Vienna, after six weeks' use of the material in all cases where he would have used iodoform, writes that dermatol is a splendid wound-healing material, best in superficial and fresh wounds, but of great value in abscesses and phlegmonous wounds that have been thoroughly opened, the necrotic tissue removed, and washed with corrosive. Such wounds clear themselves in a short time, the secretion quickly disappears, and a dry, red, granulating surface presents itself. On the whole he considers dermatol the best dry antiseptic we possess.

O. Rosenthal, in a paper before the Berlin Dermatological Society, reported cases of hard and soft chancres, balanitis, purulent lymphangitis, burns, gonorrhœa, leg ulcers, etc., all treated with this material, and all giving very satisfactory results. But the best results which he obtained were in

moist eczemas, of which he treated a large number of cases. He concludes by stating that in his opinion dermatol will prove of great value in dermatological practice.

In a later paper Rosenthal speaks of his further use of the sub-gallate of bismuth in his clinic, and states that it has fully come up to all that was anticipated of it. He claims an almost diagnostic value for it in cases of ulcers of the penis, specific ulcers healing very rapidly, while chancroids healed not nearly so rapidly as under other dressings. This latter does not coincide with my own observations.

Dr. E. Glaeser, of the gynæcological department of Breslau, considers that dermatol is no substitute for iodoform in foul, necrosing wounds, but is of great value in fresh wounds, granulating wounds and well cleansed cavities. Its superiority lies in the fact that no drying antiseptic so completely favors the primary union of aseptic wounds, especially in all plastic, and fresh post-partum and perineal wounds, where the primary union is always in danger from abundant secretion. In foul abortion cases, Glaeser still holds to the use of iodoform.

Robert Asch (Breslau) writes that, although the sub-gallate of bismuth appears to possess only slight antiseptic properties, through its eminent drying powers it is able to promote indirectly the aseptic healing of wounds, and has besides the excellence of being non-poisonous and non-irritating, and is unchanged by sterilization. In cervix tears it is much superior to iodoform, because it prevents the large amount of secretion that is usually present. On the other hand, in inoperable, sloughing carcinomata uteri where great numbers of bacteria are present, the sub-gallate is of little use. Most notably dermatol shows its powers in fresh tears of the vagina and perineal plastic operations. Here it protects the wound and stitches from being soaked. One can let silk stitches lie loosely under a thick layer of dermatol, covered with dermatol gauze, for days at a time,

and they will remain dry and without stitch abscesses. Asch has also used the dermatol gauze in vaginal tamponade and in vaginal catarrh with good results.

Bluhm has used the sub-gallate of bismuth in cervicitis, but with varying results. In other respects his results do not differ from those already quoted, and he is an enthusiastic advocate of its use in minor surgery and dermatitis.

Dornberger has used the sub-gallate of bismuth in a number of cases in a children's clinic, and reported the same. He found it of special value in cases of moist eczema, and in fifteen cases all were quite dry in one or, at the outside, two days. Burns and scalds healed quickly and with little formation of serum, and he was favorably impressed with the way that tubercular ulcerations acted under dermatol dressings; and in all cases where these dressings were used there was no appearance of dermatitis, —something of special importance in the delicate skins of children.

Dr. Powers, of New York, practically agrees with the foregoing expressions of opinion. He saw no irritation caused by the material, but on the other hand any irritation present quickly disappeared. He reports one case where symmetrical ulcers of specific origin were treated one with iodoform and one with dermatol, the latter healing in less than one third the time of the former.

Davidsohn reports the use of dermatol in fifty patients at the ear clinic in Berlin. While some of the cases improved very rapidly and a few cases improved, when before they had been unsuccessfully treated with boracic acid, on the whole he is inclined to the opinion that the results in purulent otorrhœa were no more satisfactory than those obtained by treatment with boracic acid.

Dr. F. L. Jack, of the Massachusetts Eye and Ear Infirmary, has told me that in his opinion healing was materially hastened in cases treated with the sub-gallate

of bismuth where formally he would have used boracic acid.

Prof. Everbusch of Erlangen has used the sub-gallate of bismuth in wounds of the eyeball ever since its introduction, and finds it of special value in aiding to get good results ; and he much prefers it to iodoform, which he formerly used.

None of the writers thus far quoted have seen anything to lead them to believe that the dermatol was at all poisonous. One case of diarrhœa and one of jaundice occurred in the hospital at Breslau, while the experiments were being made, but in both these cases the trouble persisted for some time after the use of the dermatol was given up. It was not considered as proved, therefore, that they were caused by the dermatol.

Dr. Weissmüller reports seven cases of ulcer of the leg where dermatol was used without success, all of which quickly healed under his own powder. While under the dermatol treatment one of the men complained of vertigo and itching skin. As there is no further mention of these symptoms, the author would have us infer that they disappeared when the use of the dermatol was abandoned ; but he does not state it. The second case was that of a woman who had a moist, painful ulcer on the foot. The author strewed dermatol over a large area. Three days later he found her in bed, temperature 39 C. ; headache, general lassitude, and without appetite. There was also itching over the whole body, and a burning eruption. On the foot there were blisters filled with serum. The dermatol was removed and his own powder substituted. Two days later the eruption was less and the burning gone, but the patient was weak, restless and sleepless, and complained of headache. At the end of four days she was able to attend to her daily duties.

My own experience began, as I have said, about the middle of September. One of my first cases was very

striking. I opened a large bubo in the groin and evacuated about four-fifths of the pus, and without waiting to wash out the remainder I packed the whole cavity with dermatol. At the first dressing, two days later, I was surprised to find only a thin, sero-purulent discharge and a good, clean, granulating surface; and a week later the patient was discharged. I found that this did not take place every time; that unless the abscess cavity was thoroughly curetted and cleaned out, the secretion of pus still persisted and the old, slow process of healing followed. Six or eight Cotting's operations for ingrowing toe-nail granulated quickly, and were so dry throughout that they allowed a very light dressing to be worn, which was a great gain for the convenience of the patient.

I laid open and curetted a sinus with multiple pockets in the neck, caused by suppurating glands. The wound was about 4 inches in length and ¾ to 1½ inches in depth. I had hoped to close the wound by sutures, but the pockets made it seem best to allow it to granulate up. So I filled the wound with dermatol, and at the end of two weeks the patient came again to see me with the wound entirely closed, it having been dressed twice in the meantime by Dr. Richardson of East Boston.

In a case of specific or tubercular diseases of the testicle, where removal was necessary, I found, on taking off the dressing on the third day, that everything was soft and moist, and the scrotum was distended with a sero-hemorrhagic fluid. Along the whole length of the wound the stitches seemed moist, and the whole appearance was that of a wound that was going to gape open in a few hours; and a general moist eczema threatened the whole scrotal surface. But the removal of as many stitches as possible and the bountiful application of dermatol made the whole skin nearly dry, at the next dressing, and enabled me to get a primary union along the cut surface. From my experience

with such cases I am sure that I should not have accomplished this result with any of the other active or inert surgical powders.

Crushed fingers heal very kindly under the powder, and the checking of the secretion tends to make the danger of infection much less. Of course, all such fingers were at first treated to a prolonged antiseptic bath.

The non-irritability of the bismuth compound may be seen from the following case. I removed a wen from a woman's head. The sac had been inflamed and was adherent, so that I was not sure I had removed all. To check possible suppuration I filled the cavity left with dermatol, and sent the woman away. For reasons known only to herself, she did not come back again for three weeks. At the end of that time, she returned and said that the wound had never closed. I looked to see what was the matter, and found the cavity full of dermatol that was nearly dry, and there were no signs of inflammatory reaction about the wound.

Sores of the penis I found could be kept dry more easily than with aristol, but I could see no gain in the time of healing, only the gain of having less secretion. The same I found true of sores in the vagina,—after one or two treatments the discharge was less; but the patients rarely stayed long enough to allow completed observation.

Superficial excoriations and burns of the first degree yield very rapidly to the use of dermatol, the surface drying quickly and thus allowing the epithelial growth to take effect; while with other dressings, the moisture often macerates the epithelial layers almost as rapidly as they are formed. A case in point is that of an old man who had been struck by a locomotive and had a large excoriation on his right shoulder. Dermatol was plentifully scattered over the surface, and over this was a dry gauze dressing, held in place by plasters. On the second day, all but a sur-

face of about an inch square was healed, and this yielded, in spite of the old man's wishes, in a few days more.

In chronic, moist eczematous ulcers of the leg, the soft, boggy skin surrounding the ulcer, after a few dermatol dressings, usually became dry and tough enough to allow the tin plates or stimulating applications to be made to the ulcer proper, to establish granulation.

Irritation of the skin, starting from the heat of a heavy dressing, I have repeatedly checked by the single application of dermatol; and moist, oozing eczema usually yielded to a few dressings of the powder.

In no case that I treated did I see any signs of poisoning, either local or general, although half a dram to a dram was repeatedly used, and I was spared the mortification of having to battle with an almost irresistible dermatitis, something that never happened to me before in the same length of time of out-patient service.

Dermatol I found absolutely useless to start granulation in any case where the wound has become sluggish. Indeed, in all such cases it tends to increase the trouble.

One thing must be guarded against. A thick, dry crust of serum and dermatol may form over a wound, and make a perfect little culture chamber for any bacteria which may chance to be on the surface of the wound below. And an accumulation of pus may thus be pent in below the crust, when externally the wound looks to be in a perfect condition.

My clinical observations having on the whole coincided with the work of the men whom I have already quoted, my next point was to carry out some laboratory experiments, to see whether the dermatol really hindered bacterial growth, or acted simply by its (so to speak) mechanical astringent properties, checking secretion and thus depriving the plants of the moisture necessary for their development.

The results of those who have already experimented with dermatol on its bacterial side may be summarized as follows:

(1) Bacteria, mixed with the dry powder and allowed to stand for twenty-four hours, grow when planted on agar or gelatine; though in an experiment, where a mass of staphylococcus pyogenes aureus was mixed with dermatol and put into a pocket beneath the skin of a rabbit, no abscess resulted, while in the "control", when the aureus alone was used, an abscess developed in the usual time.

(2) Thread experiments gave no better results than the control, when inert powder was used.

(3) When the sub-gallate of bismuth was mixed with galatine or agar, growth usually took place unless the amount of dermatol present was very large, when it was partially or wholly checked.

(4) When dry dermatol was strewn on the surface of tubes of gelatine or agar which had been planted with bacteria, the results have differed. In many cases no growth appeared; in others apparently no hindrance to growth was present. Bluhm gives a list of twelve different varieties of bacteria which he has experimented with, and his results were decidedly in favor of the destruction from the dermatol. In many cases he was unable to find live bacteria on the surface after a few days.

(5) Bluhm also obtained positive results of the retarding action of the dermatol in tubes where the nutrient medium had been colored with an indigo-carmine solution, which is decolorized by the products of bacterial growth. The color disappeared in the control tubes on the third day, and in the dermatol tubes from the tenth to the fifteenth day, according to the amount of the powder used. In these experiments the absence of air was secured.

(6) In fluids the growth of bacteria was not influenced, so far as was observed, by the presence of the dermatol.

The late Dr. John A. Jeffries, in his able paper on the Antibacteriological Action of Iodoform, exposed the fallacy of deductions made from tube and thread experiments. He

also showed that iodoform did have some effect in checking bacterial growth, and suggested as an explanation of this, that was later confirmed by Behring in Germany, that the favorable action of iodoform was doubtless due to its chemical combination with various products of bacterial growth, —the so-called ptomains. I shall endeavor to show that a similar change takes place when bacteria are grown in the presence of the sub-gallate of bismuth.

In the first set of experiments I planted four gelatine tubes with pus from a newly opened abscess, and keeping a control tube, dusted the surface of the other tubes respectively with iodoform, aristol and dermatol. No difference could be seen in the rapidity with which the bacteria grew and liquified the gelatine in all the tubes.

A series of experiments were made where the sub-gallate of bismuth and iodoform were added to equal amounts of melted gelatine and agar. The contents of the tubes were then cooled so that the powder should be mixed as thoroughly as possible through the nutrient media, when cooled. In some half dozen comparative series, I found that there was practically but little difference in the amount of growth on the variously modified media. Sometimes the growth appeared equal in all respects to the control, while at others there was a marked hindrance to the growth.

In several instances there was a change of color produced by the presence of either dermatol or iodoform. This was most marked in one case, where an orange coccus, grown on gelatine and dermatol, became a dark brown, and the same plant, grown on gelatine with iodoform, lost its color and was white. Planting again on agar, the brown returned at once to its original orange, while the plant grown on iodoform only showed traces of color in the second generation. In another case, where I planted a white coccus taken from a wound, probably a staphylococcus pyogenes albus, on gelatine to which dermatol had been added, the

liquefied portion became gray, and finally inky black, due in all probability to the presence of the sulphide of bismuth.

These observations go to show that bacteria grown in the presence of sub-gallate of bismuth and iodoform are able to change the chemical combination of the powders present; and in order to bring about this change, it is fair to suppose that the products of bacterial growth, the so-called ptomains, are also changed.

CULTURE TUBE EXPERIMENTS.

GELATINE.	CONTROL.	DERMATOL.	IODOFORM.
Staphylococcus pyogenes aureus. (?)	Slow growing, liquefying the gelatine. Color, light orange.	Strong growth, slow liquefying. Color, dark brown.	Fair growth, slow growing, slightly liquefying, white.
Mixed culture from pus.	Slowly liquefying. Color, yellow and white.	Less liquefaction. Color, brown.	Thin line of growth. Color, white.
Pus from suppurating wound.	Growing and liquefying with equal rapidity.		
Albus (?) from sloughing wound.	Rapid growth, liquefying.	Growth and liquefaction more slow than control. Fluid gray; later, black.	More slow than control, no change in color.
Light yellow coccus from syphilitic testicle.	Heavy and rapid yellow growth.	Very slight growth. Color, yellow.	Growth about like control. Color white.
Deep orange coccus.	Small growth, not liquefying.	Very slight growth. Brighter orange.	No growth.
Agar agar tubes. Red yeast.	Small growth.	Less growth.	
Aureus.	Heavy growth.	No growth.	
Crookshanks.	Good growth, color only at edges at first.	Equal growth. Color, stronger; later, fading.	
Green pus bacillus.	Good growth, mass of bacilli white.	Tube a, b } Growth like control. Tube c } Mass of bacilli black.	
Staphylococcus cereus flavus.	Heavy yellow growth.	Tube a } Very slight growth. Tube b } No growth. Tube c } Less than control, mould contamination.	
Gelatine tubes planted with pus from abscess of the hand and the powd'rs dusted on	All grew and liquefied the gelatine with equal rapidity.		

As the ptomains are now recognized as the probable cause of septic conditions, and as frequently the poisonous differ from the innocuous only by the change of the arrangement of a few atoms, the fact that the modification of the

ptomains does occur is a fact of importance in considering the merits of any antiseptic powder.

QUANTITATIVE EXPERIMENTS.

Remarks.	Control. 1st 5 estimated.	Dermatol.	Iodoform.
In first five experiments, .5 c. g. dermatol or iodoform used.	32,400 colonies.	Sterile. Sterile. 5 colonies.	1123 1991 2475 } Colonies.
Same as ex. 1. 24 hours later.	12,600 colonies. Diminution due	Sterile. Sterile. to starvation in dis	336 142 } Colonies. tilled water (?).
	9,020 colonies.	2 colonies. 28 colonies.	1920 colonies.
Same bouillon tubes, 5 days later.	23,400 colonies.	2937 colonies.	2194 colonies.
	Heavy growth.	2 colonies. 1 colony.	Plate spoiled.
.2 c. g. used yellow coccus from syphilitic testicle.	Plate destroyed.	Sterile.	
Aureus, old culture.	233	3	
Crookshank's purple.	One large colony.	Sterile.	
Aureus, recent culture.	10,000 estimate.	Sterile.	
Albus.	50	Sterile.	
.3 c. g. used. Staphylococcus cereus flavus.	82 large colonies.	a. 61 small colonies. b. Sterile. c. Sterile.	
Green pus.	Very heavy growth.	a, b, c } Very heavy growth.	
Anthrax.	Heavy growth.	6 colonies.	

I lastly made a number of quantitive experiments, following the line of Dr. Jeffries in which he obtained most positive results in his work on iodoform. My method was as follows: I added a small number of bacteria to tubes containing 10 c.c. of bouillon, and bouillon to which equal amounts of iodoform and dermatol had been added, and let the tubes of the same series remain under similar conditions, *i.e.*, some series remained 24 to 48 hours in the constant temperature apparatus; others stood at the room temperature; and some were left partly at room temperature and partly in the thermostat. When ready, I took accurately measured amounts from each of these tubes and added this to tubes containing 10 c.c. of sterilized water; and taking a measured amount of this dilution, I added it to agar tubes

where the agar was just on the point of cooling, and made agar plates. These plates remained in the thermostat a sufficient time, and the colonies were then counted. By this means I was able to get a fairly accurate quantitive result, and a comparison between the free growing bacteria and those grown in the presence of iodoform and dermatol.

The conclusions that I have drawn from my investigations are, that the sub-gallate of bismuth, called dermatol from its astringent properties in checking secretion—also, its odorless, non-irritating, non-poisonous properties—has proved itself to be a valuable addition to the surgeon's armamentarium. And the laboratory experiments show that in addition to its mechanical power of repelling water, and thus producing a food famine and consequent death of many of the bacteria, that it has active powers in hindering bacteria growth, although it does not have bacteriacidal action. The method by which this hindrance is accomplished is probably due to its chemical combination with the ptomains produced by the growth of the bacteria, forming compounds hostile to their rapid development.

NOTE.—I use the word ptomains according to the definition of Brieger, and they include all nitrogenous bases that are formed by the action of bacteria.

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